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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
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EXAMINER	
PENN, M	
ART UNIT	PAPER NUMBER
1633	5

DATE MAILED: 04/04/01

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Offic Action Summary	Application No. 09/559,327	Applicant(s) DURING, MATHEW JOHN	
	Examiner Michael G. Penn	Art Unit 1633	

-- The MAILING DATE of this communication appears on th cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____ .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) 1-12 is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) 1-12 is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

15) ☒ Notice of References Cited (PTO-892)
16) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
17) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 2 .
18) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
19) ☐ Notice of Informal Patent Application (PTO-152)
20) ☐ Other:

DETAILED ACTION

Specification

1) The first line of the specification must specify that this application is a continuation of application 08/472,755, now abandoned.

2) Figure 1 description (page 2, line 12) should begin with Fig. 1A-1C.

3) Figure 2 description (page 2, line 19) should begin with Fig. 2A-2B.

Claims 1-12 are pending and under consideration in the instant office action.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1-6, 8, and 10-12 of the instant application refer to delivery of an AAV vector to the gut, whereas claims 1-8 of U.S. Patent No. 6,110,456 refer to delivery of an AAV vector to the small intestine. The gut of an animal as claimed encompasses the

small intestine as in the claims of U.S. Patent No. 6,110,456. Therefore, the claims of 6,110,456 obviate the claims of the instant application.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-12 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of obtaining production of a protein in cells of the small intestine epithelium of an animal, does not reasonably provide enablement for producing a protein anywhere in the gut as broadly claimed. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

The claims recite producing protein anywhere in the gut of an animal. While progress has been made in recent years for gene transfer *in vivo*, vector targeting to desired tissues *in vivo* continues to be unpredictable and inefficient as supported by numerous teachings available in the art. For example, Miller (1995, FASEB J., Vol. 9, pages 190-199) review the types of vectors available for *in vivo* gene therapy, and conclude that "for the long-term success as well as the widespread applicability of human gene therapy, there will have to be advances...targeting strategies outlined in this review, which are currently only at the experimental level, will have to be translated

into components of safe and highly efficient delivery systems" (page 198, column 1). Deonarain (1998, Expert Opin. Ther. Pat., Vol. 8, pages 53-69) indicate that one of the biggest problems hampering successful gene therapy is the "ability to target a gene to a significant population of cells and express it at adequate levels for a long enough period of time" (page 53, first paragraph). Deonarain reviews new techniques under experimentation in the art which show promise but states that such techniques are even less efficient than viral gene delivery (see page 65, first paragraph under Conclusion section). Verma (Sept. 1997, Nature, Vol. 389, pages 239-242) reviews vectors known in the art for use in gene therapy and discusses problems associated with each type of vector. The teachings of Verma indicate a resolution to vector targeting has not been achieved in the art (see entire article). Verma also teaches appropriate regulatory elements may improve expression, but it is unpredictable what tissues such regulatory elements target (page 240, sentence bridging columns 2 and 3). Crystal (1995, Science, Vol. 270, page 404-410) also reviews various vectors known in the art and indicates that "among the design hurdles for all vectors are the need to increase the efficiency of gene transfer, to increase target specificity and to enable the transferred gene to be regulated" (page 409). Therefore, the state of the art at the time of filing was that it was unpredictable how to target DNA to cells of interest.

Applicant has taught oral administration of an AAV vector comprising a gene encoding β-galactosidase results in β-galactosidase expression in lamina propria cells and possibly intestinal brush-border cells of the small intestine, with expression of said gene resulting in amelioration of a lactase deficiency. However, applicant has not

clearly taught expression of the vector in cells of other organs of the gut besides the small intestine. Therefore, the claims should be limited to obtaining expression in the small intestine. Moreover, considering the physiological differences between cells of the small intestine (which are adapted to take up materials from the digestive tract), cells of the stomach (which are adapted to secrete digestive enzymes and acids), and the large intestine (which are adapted to absorb water from the digestive tract), one skilled in the art would have reason to doubt an unsupported assertion that a vector which transduces small intestine cells would succeed in transducing cells throughout the entire gut (as in claims 1-12).

Furthermore, considering the lack of evidence of cell transduction in the large intestine, and the lack of evidence of AAV viability when incorporated in a suppository formulation, one would have reason to doubt unsupported assertions of effective delivery of the vector in suppository form (as in claim 7).

In regard to antisense nucleic acids and genetic control elements, effective use of antisense materials requires delivery of the antisense nucleic acid to the appropriate subcellular location of the appropriate cells, in amounts large enough to suppress the expression of an endogenous gene. Effective use of a genetic control element further requires association between the control element and the target gene. Considering the difference between the working examples showing biological activity of a catalytic enzyme, and the requirements for effective use of an antisense RNA or a genetic control element, one skilled in the art would have reason to doubt unsupported assertions of effective use of these types of materials.

Considering the limited guidance in the specification, the broad scope of the claims, the limited scope of the working examples, and the unpredictability of extrapolating results from one type of experiment to other tissues, other delivery formulations, and other types of expressed products, it is maintained that undue experimentation would be required to practice the full scope of the invention as claimed.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 12 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 12 is vague and indefinite because it is not clear what is intended by a "β-galactose gene and promoter system," or what components (i.e. promoter sequences or other nucleic acid elements) would be considered in the construction of such a system. Deleting the phrase "wherein said DNA..." and replacing it with "wherein said gene of interest is a β-galactose gene operatively linked to a promoter" would overcome this rejection.

Claim 12 recites the limitation "said DNA segment" in claim 1. There is insufficient antecedent basis for this limitation in the claim.

No claims are allowed.

Inquiry concerning this communication or earlier communications from the examiner should be directed to Michael G. Penn who can normally be reached on Monday through Friday from 8:00 am to 4:30 p.m. at (703) 308-2454.

Questions of formal matters can be directed to the patent analyst, Kimberly Davis, who can normally be reached on Monday through Friday from 9:00 am to 5:30 PM at (703) 305-3015.

Questions of a general nature relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-1235.

If attempts to reach the examiner, patent analyst or Group receptionist are unsuccessful, the examiner's supervisor, Deborah Clark, can be reached on (703) 305-4051.

The official fax number for this Group is (703) 308-4242.

Michael G. Penn

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